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MATTERS ARISING

Diagnosis of genital human papillomavirus lesions in the male

In an excellent study by Hippeläinen *et al*[1] the histopathological criteria for HPV infection were evaluated. As the authors point out HPV DNA may be detected in tissue lacking histopathological HPV associated signs and so can also the opposite situation occur.

Out of the HPV DNA negative biopsies (in situ hybridisation (ISH) technique) 26·7% did show koilocytosis, a sign said to be linked to a replicative HPV infection. The conclusion that koilocytosis is the strongest predictor for HPV positivity in flat genital lesions, giving a risk ratio of 3·7, is worthy of note but it would be interesting to hear the authors further discuss the finding of koilocytosis in the HPV DNA negative patients and the completely normal histology in the adjacent biopsied area. Were no pathological signs found at all? HPV are known to be latent in clinically normal tissue.[2]

As for the characteristic vacuolisation, also mentioned to be associated to HPV infection, maybe it should be discussed since it could be misinterpreted as koilocytosis by the pathologists not familiar with the signs of HPV infection. In the study referred to vacuolisation was more frequent in HPV negative cases than in HPV positive ones. This inverse correlation is only noticeable in table 4 but is for certain of interest. The authors conclude that HPV typing is essential for diagnosis in doubtful cases (lacking koilocytosis). We want to point out the fact that there is a diagnostic difficulty also in the case where koilocytosis is present and the rather insensitive ISH is negative.

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1 Hippeläinen MI, Syrjänen S, Hippeläinen MJ, Saarikoski S, Syrjänen K. Diagnosis of genital human papillomavirus (HPV) lesions in the male: correlation of peniscopy, histology and in situ hybridisation. *Genitourin Med* 1993;**69**:346–51.
2 Ferenczy A, Mitao M, Nagai N, Silverstein SJ, Crum CP. Latent papillomavirus and recurring genital warts. *N Engl J Med* 1985;**313**: 784–8.

Hippeläinen et al reply:

While opening the discussion about our recent paper,[1] Drs Strand and Rylander focused on an important issue; the concordance between histology and HPV DNA typing in genital HPV lesions. Indeed, the sometimes low concordance between these two techniques as a source of diagnostic problems has been emphasised in the female genital lesions as well, but according to our experience, such a discordance seems to be an even more severe problem in the diagnosis of genital HPV infections in the males.

In the present series, a type-specific in situ hybridisation (ISH) with seven different probes (HPV 6,11,16,18,31,33,42) was used as the detection method of HPV DNA.[1] As shown in table 4, the two morphological signs in the biopsies most frequently associated with HPV DNA-positivity were koilocytosis (67·6%) and acanthosis (61·7%). However, these two histological features were detected in HPV DNA-negative biopsies as well, that is, in 26·7% and 40·4% of cases, respectively. As pointed out by Strand and Rylander, koilocytosis is generally accepted as the cytopathic effect of HPV, being the hallmark of a productive HPV infection.

However, in diagnostic studies like this, it is frequently impossible to discover the specific HPV type inducing the koilocytotic change in all tissue biopsies, that is, to achieve a 100% correlation between morphology and presence of HPV DNA. This has multiple reasons. The two most feasible ones to explain the situation in the present series include the following: (1) Of the currently recognised 71 different HPV types, more than 30 are known to infect the genital mucosa. If all these probes are not included in the diagnostic test panel, it is more than probable that a minor or major proportion of the biopsy specimens analysed remain HPV DNA-negative. Our test panel included the seven most frequent HPV types, covering usually some 70% of the HPV-positive samples in most series.[2] (2) Albeit a highly applicable diagnostic tool, ISH has its limitations, namely, its sensitivity of approximately 20 viral copies/cell. Accordingly, any cell harbouring HPV DNA copies below that limit, most likely remains undetected by ISH. For some unknown reason, the viral load in the male genital HPV lesions seems to be substantially lower than that in the female HPV lesions, which might be one of the reasons why HPV DNA-detection rate by ISH is significantly higher in the latter.

The latter point (2) is also pertinent to the second issue raised by Strand and Rylander; the detection of HPV DNA in histologically normal epithelium. Of the 135 biopsies classified as normal on light microscopy, HPV DNA was found in nine (6·7%) (table 4). This is in agreement with the concept on latent HPV infections, the diagnostic criteria of which were recently outlined in detail.[3]

The third subject pointed out in their letter is the difficulty in making the distinction between true koilocytes and vacuolised cells. The former are considered as the cytopathic sign of HPV, the latter most probably arise as a result of multiple non-specific stimuli. In fact, such vacuolised cells were rare (6·9%) in HPV DNA-positive lesions, but more frequent (14·7%) in HPV DNA-negative biopsies. We completely agree with Strand and Rylander in their statement that the correct diagnosis of male genital HPV lesions is sometimes difficult both in cases with and without koilocytosis, even if you have ISH in use. It is good to remember, however, that even more difficult problems (albeit of different character) may arise, if more sensitive HPV DNA detection techniques, such as PCR are used.

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1 Hippeläinen MI, Syrjänen S, Hippeläinen MJ, Saarikoski S, Syrjänen K. Diagnosis of genital human papillomavirus (HPV) lesions in the male: correlation of peniscopy, histology and in situ hybridization. *Genitourin Med* 1993;**69**:346–51.
2 Kataja V, Syrjänen K, Syrjänen S, *et al.* Prospective follow-up of genital HPV infections: Survival analysis of the HPV typing data. *Eur J Epidemiol* 1990;**6**:9–14.
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NOTICES

The UK Family Planning Association

The UK Family Planning Association is beginning a research project to explore the development of recent family planning and reproductive health initiatives within the UK. We particulrly wish to gather information from people currently or recently associated with clinical facilities which combine access to family planning information and services with genitourinary medicine and sexual health provision. In the first instance we wish to invite health and social welfare professionals with experience of planning, developing, managing or working in combined clinic services to contact:
Joan Walsh
Health Policy and Research Officer
Family Planning Association
27–35 Mortimer Street
London W1N 7RJ, UK
Tel: 071 636 7866

Fifth Congress of the European Academy of Dermatology. 13–17 October 1996. Lisbon, Portugal

Further information may be obtained from: Professor A. Cabral Ascensão, Clinica Universitária de Dermatologia e Venereologia, Hospital Pulido Valente, Alam. Linhas de Torres, 1700 Lisboa, Portugal.

IUVDT World STD/AIDS Congress 1995. 19–23 March 1995, Singapore

For further information contact: Communication Consultants, 336 Smith Street #06-302, New Bridge Centre, Singapore 0105. Telephone (65) 227 9811. Fax (65) 227 0257.

CURRENT PUBLICATIONS

Selected titles from recent reports published worldwide are arranged in the following sections:

Gonorrhoea
Chlamydia
Pelvic inflammatory disease
Candidiasis
Bacterial vaginosis
Trichomoniasis
Syphilis and other treponematoses
Hepatitis
Herpes
Human papillomavirus infection
Cervical cytology and colposcopy
Other sexually transmitted diseases
Public health and social aspects
Microbiology and Immunology
Dermatology
Miscellaneous

Gonorrhoea

Multicenter trial of single dose azithromycin vs ceftriaxone in the treatment of uncomplicated gonorrhoea.
HH HANDSFIELS, ZA DALU, DH MARTIN, *et al.* *Sex Transm Dis* 1994;**21**:107.

Bactericidal activity of six antibiotics against *Neisseria gonorrhoeae*.
Y CRENN, M MEYRAN, T SAMSON, JD CAVALLO. *J Antimicrob Chemother* 1994;**33**:855.

Variation in hydrogen peroxide sensitivity between different strains of *Neisseria gonorrhoeae* is dependent on factors in addition to catalase activity.
TM ALCORN, HY ZHENG, MR GUNTHER, DJ HASSETT, MS COHEN. *Infect Immun* 1994;**62**: 2138.

Chlamydia

Risk factors for recurrent *Chlamydia trachomatis* infections in women.
SD HILLIS, A NAKASHIMA, PA MARCHBANKS, DG ADDISS, JP DAVIS. *Am J Obstet Gynecol* 1994; **170**:801.

Chlamydia serologic studies and recurrent spontaneous abortion.
R RAE, IW SMITH, WA LISTON, DC KILPATRICK. *Am J Obstet Gynecol* 1994;**170**:782.

Genital chlamydial infection; diagnostic practices of general practitioners in Melbourne, Australia.
F WESTGARTH, N CROFTS, DM GERTIG. *Sex Transm Dis* 1994;**21**:118.

Factors associated with the geographic variation of reported chlamydia infection in Minnesota.
EA BELONGIA, SJ MOORE, RS STEECE, KL MACDONALD. *Sex Transm Dis* 1994;**21**:70.

A randomized, prospective trial comparing amoxicillin and erythromycin for the treatment of *Chlamydia trachomatis* in pregnancy.
NS SILVERMAN, M SULIVAN, M HOCHMAN, M WOMACK, DL JUNGKIND. *Am J Obstet Gynecol* 1994;**170**:829.

Urine as an alternative to urethral swabs for the diagnosis of *Chlamydia trachomatis* in infertile males.
TN RAMUTHAGA, MS BORNMAN, M MAHOMED, D BOOMKER, AS GREEF, HH CREWEBROWN, S REIF. *Int J Andrology* 1994;**17**:9.

Non-invasive sampling for detection of genital infection with *Chlamydia trachomatis* in males utilising urinary leukocyte esterase tests and immunoassays.
MA DOMEIKA, M BASSIRI, PA MARDH. *Infection* 1994;**22**:65.

Oral contraceptives do not alter the course of experimentally induced chlamydial salpingitis in monkeys.
DL PATTON, YTC SWEENEY, CC KUO. *Sex Transm Dis* 1994;**21**:89.

Antibody recognition of a neutralization epitope on the major outer membrane protein of *Chlamydia trachomatis*.
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Interaction of the *Chlamydia trachomatis* histone H1-like protein (Hc1) with DNA and RNA causes repression of transcription and translation in vitro.
LB PEDERSEN, S BIRKLUND, G CHRISTIANSEN. *Mol Microbiol* 1994;**11**:1085.

Pelvic inflammatory disease

Epidemiology of pelvic inflammatory disease.
F GRODSTEIN, KJ ROTHMAN. *Epidemiol* 1994;5: 234.

Observations concerning the microbial etiology of acute salpingitis.
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Candidiasis

Detection of anti-*Candida albicans* IgE antibodies in vaginal washes front patients with acute vulvovaginal candidiasis.
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Effects of preinduced candida-specific cell-mediated immunity on experimental vaginal candidiasis.
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Adherence of *Candida albicans* to endothelial cells is inhibited by prostaglandin I-2.
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Mechanisms by which *Candida albicans* induces endothelial cell prostaglandin synthesis.
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The role of microfilaments and microtubules during pH-regulated morphological transition in *Candida albicans*.
K YOKOYANA, H KAJI, K NISHIMURA, M MIYAJI. *Microbiology* 1994;**140**:281.

Bacterial vaginosis

Bacterial vaginosis—efficacy and safety of intravaginal metronidazole treatment.
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Trichomoniasis

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R MURESU, S RUBINO, P RIZZU, A BALDINI, M COLOMBO, P CAPPUCCINELLI. *J Clin Microbiol* 1994;**32**:1018.

Syphilis and other treponematoses

Epidemic syphilis: maternal factors associated with congenital infection.
BL MCFARLIN, SF BOTTOMS, BS DOCK, NB ISADA. *Am J Obstet Gynecol* 1994;**170**:535.

A case of secondary syphilis combining classical and atypical features.
Z DAMANHOURY, EL SMITH. *Eur J Dermatol* 1994;**4**:159.

HIV and syphilis seroprevalence among clients with sexually transmitted diseases attending a walk-in clinic at Cook County Hospital.
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K WICHER, F ABBRUSCATO, V WICHER, L SCHOULS. *Int Arch Allergy Immunol* 1994;**103**: 396.

Hepatitis

Research in chronic viral hepatitis.
Archives of Virology Supplement 8; 1993 (whole issue).

Spousal transmission of the hepatitis C virus?
LB SEEFF, HJ ALTER. *Ann Intern Med* 1994;**120**: 807.

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SJ SKIDMORE, KE COLLINGHAM, SM DRAKE. *J Med Virol* 1994;**42**:247.

Hepatitis C virus infection in a sexually active inner city population. The potential for heterosexual transmission.
GL DAIKOS, S LAI, MA FISCHI. *Infection* 1994;**22**: 72.

Hepatitis B virus infection in a group of heterosexuals with multiple partners in Amsterdam, The Netherlands: implications for vaccination?
GJJ VANDOORNUM, HJA VANHAASTRECHT, C HODYKASS, *et al. J Med Virol* 1994;**43**:20.

Herpes

Analysis of the epidemiology and pathogenesis of herpes simplex virus infections in pregnant women and infants using the HSV-2 glycoprotein G antibody assay.
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Seroprevalence of antibodies to human herpes viruses in England and Hong Kong.
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Autopsy findings in two cases of neonatal herpes simplex virus infection: detection of virus by immunohistochemistry, in situ hybridization and the polymerase chain reaction.
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A DE RUITER, RN THIN. *Drugs* 1994;**47**:297.

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SD CHAMBERLAIN, AR MOORMAN, TC BURNETTE, P DEMIRANDA, TA KRENITSKY. *Antivir Chem Chemother* 1994;**5**:64.

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Human papillomavirus infection

The absence of vaginal human papillomavirus 16 DNA in women who have not experienced sexual intercourse.
E RYLANDER, L RUUSUVAARA, MW ALMSTROMER, M EVANDER, G WADELL. *Obstet Gynecol* 1994; **83**:735.

Low concordance of genital human papillomavirus lesions and viral types in HPV-infected women and their male sexual partners.
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Detection of human papillomavirus by the polymerase chain reaction in histologically normal penile skin adjacent to penile warts.
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Risk of genital human papillomavirus infection in women with human immunodeficiency virus induced immunosuppression.
GYF HO, RD BURK, I FLEMING, RS KLEIN. *Int J Cancer* 1994;**56**:788.

Typing of human papillomaviruses in condylomata acuminata from Greece.
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Prevalence of HPV in premalignant and malignant cervical lesions in Greenland and Denmark; PCR and insitu hybridization analysis on archival material.
AM SEBBELOV, C SVENDSEN, H JENSEN, SK KJAER, B NORRILD. *Res Virol* 1994;**145**:83.

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Sexually transmitted diseases and other risk factors for cervical dysplasia among southwestern Hispanic and non-Hispanic white women.
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Absence of human papillomavirus in squamous cell carcinomas of nongenital skin from immunocompromised renal transplant patients.
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